

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference 61386PCT.(72021)	<b>FOR FURTHER ACTION</b>	See item 4 below
International application No. PCT/US2005/006697	International filing date ( <i>day/month/year</i> ) 01 March 2005 (01.03.2005)	Priority date ( <i>day/month/year</i> ) 04 March 2004 (04.03.2004)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant NEUROGEN CORPORATION		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).
  2. This REPORT consists of a total of 6 sheets, including this cover sheet.
- In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- |                                     |              |   |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I    | Basis of the report   |
| <input type="checkbox"/>            | Box No. II   | Priority  |
| <input checked="" type="checkbox"/> | Box No. III  | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability  |
| <input type="checkbox"/>            | Box No. IV   | Lack of unity of invention  |
| <input checked="" type="checkbox"/> | Box No. V    | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/>            | Box No. VI   | Certain documents cited   |
| <input type="checkbox"/>            | Box No. VII  | Certain defects in the international application  |
| <input type="checkbox"/>            | Box No. VIII | Certain observations on the international application   |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No. +41 22 338 82 70	Date of issuance of this report 05 September 2006 (05.09.2006)  Authorized officer <p style="text-align: center; font-weight: bold;">Philippe Becamel</p> e-mail: pt12@wipo.int
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# PATENT COOPERATION TREATY

REC'D 20 JUL 2005

From the  
INTERNATIONAL SEARCHING AUTHORITY

WIPO

PCT

## PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To:  
JOHN B. ALEXANDER  
EDWARDS & ANGELL, LLP  
P.O. BOX 55874  
BOSTON, MA 02205

Date of mailing  
(day/month/year) **18 JUL 2005**

Applicant's or agent's file reference

**FOR FURTHER ACTION**

See paragraph 2 below

61386PCT(72021)

International application No.

International filing date (day/month/year)

Priority date (day/month/year)

PCT/US05/06697

04 March 2005 (04.03.2005)

04 March 2004 (04.03.2004)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): A61K 31/395, 31/505; C07D 215/16, 239/95. and US Cl.: 514/266.21, 266.4, 232.8, 299; 544/116, 230, 231, 284 and 293.

Applicant

NEUROGEN CORPORATION

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

### 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US

Mail Stop PCT, Attn: ISA/US  
Commissioner for Patents  
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International application No.

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Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

- ☐ This opinion has been established on the basis of a translation from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

- ☐ a sequence listing  
☐ table(s) related to the sequence listing

b. format of material

- ☐ in written format  
☐ in computer readable form

c. time of filing/furnishing

- ☐ contained in international application as filed.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

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INTERNATIONAL SEARCHING AUTHORITY

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application  
☒ claims Nos. 1-11, 17-25, 29-39 and 43-96

because:

- ☒ the said international application, or the said claim Nos. 49-96 relate to the following subject matter which does not require an international preliminary examination (*specify*):

Claims 49-50 are drawn to a pharmaceutical composition. Claims 51-96 are drawn to various methods of treatment or use. The search has been carried out and based on the alleged effects of the compounds; therefore, the written opinion is only for the alleged effects of the compounds as well.

- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-11, 17-25, 29-39 and 43-48 are so unclear that no meaningful opinion could be formed (*specify*):

Please See Continuation Sheet

- ☐ the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported by the description that no meaningful opinion could be formed.

- ☒ no international search report has been established for said claims Nos. 1-11, 17-25, 29-39 and 43-96.

- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐

has not been furnished

☐

does not comply with the standard

the computer readable form

☐

has not been furnished

☐

does not comply with the standard

- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

- ☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.  
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Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>NONE</u>	YES
	Claims <u>12-16, 26-28 and 40-42</u>	NO
Inventive step (IS)	Claims <u>NONE</u>	YES
	Claims <u>12-16, 26-28 and 40-42</u>	NO
Industrial applicability (IA)	Claims <u>12-16, 26-28 and 40-42</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 12-16, 26-28 and 40-42 lack an inventive step under PCT Article 33(3) as being obvious over Hackler et. al. (US 5,034,393). On columns 1-2, Hackler et. al. disclose a generic formula (1) which encompasses compounds claimed herein; particularly, when the disclosed formula has the following substituents:

One or two of A, B, E or D are N, and the others are CR<sup>1</sup>;  
R<sup>1</sup> can be phenyl or substituted phenyl, which corresponds to the instant variable Ar;  
X can be NR<sup>1</sup>;  
Y can be a bond or an alkylene chain;  
Z can be a phenyl group of the formula (2).

Although no species with said substituents are taught, the clearly defined scope of formula (1) in US'393 would have provided sufficient motivation for one of the ordinary skill in the art to select and make the compounds recited herein. Therefore, at the time the invention was made, it would have been obvious to one skilled in the art to make the claimed compounds in view of the genus taught by Hackler et. al.

Claims 12-16, 26-28 and 40-42 also lack novelty under PCT Article 33(2) for the reason stated above.

Claims 12-16, 26-28 and 40-42 meet the criteria set out in PCT Article 33(4), and thus they have industrial applicability because the subject matter claimed can be made or used in the pharmaceutical industry.

WRITTEN OPINION OF THE  
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Supplemental Box  
In case the space in any of the preceding boxes is not sufficient.

Section III. Non-establishment of opinion (description/claims/drawings unclear)

Claims 1, 17, and 32 are independent claims drawn to compounds of a bicyclic system substituted with a ring containing  $A_1-A_5$ . Variables  $A_1-A_5$  are defined in terms of N or  $CR_a$ . Variable  $R_a$  is defined in terms of hydrogen,  $R_b$  and "*groups that are taken together with an adjacent  $R_a$  to form a...ring.*" It is unclear what "*groups*" are taken together. Furthermore,  $R_a$  can also form a ring with  $R_3$ , and thus, it is unclear if a tricyclic system is also intended for the fused ring containing  $A_1-A_5$ . Because of the ambiguity in the definitions of  $R_a$  and  $A_1-A_5$ , and the uncertainty in the number of rings, no meaningful search can be carried out for the compounds recited in claims 1, 17 and 32. Therefore, no meaningful opinion can be formed for these claims.

Claims 2-11, 18-25, 29-31, 33-39 and 43-48 depend on claim 1, or 17 and/or 32 for the definition of  $R_a$ , and the ring containing  $A_1-A_5$ , and thus, the compounds recited in said claims cannot be searched or examined either.

Claims 52-61, 63, 65-67, 69-71, 73-79, 81, 83, 85 and 87 are improper multiple dependent claims.